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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,337	07/26/2001	Satoshi Mori	55107	5232
21874	7590	03/23/2006		
EDWARDS & ANGELL, LLP			EXAMINER	
P.O. BOX 55874			FRONDA, CHRISTIAN L	
BOSTON, MA 02205				
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 03/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/674,337	MORI ET AL.
	Examiner	Art Unit
	Christian L. Fronda	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 23 November 2005.  
 2a) This action is FINAL. 2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,3 and 27-57 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) 1,35-38 and 41 is/are allowed.  
 6) Claim(s) 3,27,28,31-34,40,42-44,47-49,52-54 and 57 is/are rejected.  
 7) Claim(s) 29,30,39,45,46,50,51,55 and 56 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 26 July 2001 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date 11/23/05.

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_.  
 5) Notice of Informal Patent Application (PTO-152)  
 6) Other: \_\_\_\_\_.

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## DETAILED ACTION

1. Claims 1, 3 and 27-57 are pending and under consideration in this Office Action.

### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
3. Claims 3, 27, 28, 31-34, 40, 42-44, 47-49, 52-54, and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nicotianamine synthase comprising an amino acid sequence that has more than 90% amino acid identity to SEQ ID NO: 1; does not reasonably provide enablement for an enzyme comprising an amino acid sequence that has at least 50%, amino acid sequence identity to SEQ ID NO: 1 comprising any of the consensus amino acid sequences depicted in said claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicants' arguments filed 11/23/2005 have been fully considered. Applicants' position is that in situations where an amino acid sequence is isolated from a natural source, one of skill in the art need not be taught which amino acid residue(s) can be changed without inactivating enzyme activity. Applicants argue that the attached Declaration of Dr. Satoshi Mori filed 11/23/2005 shows conserved sequences which would indicate positions where conservative changes can be made. Applicants state amino acid identities of 47.5%, 44.1%, 48.5%, and 49% identity were found between SEQ ID NO: 1 and nicotianamine synthases of AtNAS1, AtNAS2, ATNAS3, and AtNaS4, respectively. Applicants argue that since methods for isolating, mutating, and testing for nicotianamine synthases have been disclosed in the specification, then any testing needed to identify or confirm suitable nicotianamine synthases is well within routine experimentation.

The examiner appreciates applicants' arguments and agrees that an isolated nicotianamine synthase that has 90% amino acid identity to SEQ ID NO: 1 is enabled by the specification. However, the examiner respectfully disagrees with applicants' position that claims encompassing

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50% identity to SEQ ID NO: 1 are not enabled by the specification for the reasons of record as supplemented below.

As stated in the previous Office Action the standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. While the Declaration of Dr. Satoshi Mori filed 11/23/2005 shows an alignment of several nicotianamine synthases and that several nicotianamine synthase were found to have amino acid identities of 47.5%, 44.1%, 48.5%, and 49% identity to SEQ ID NO: 1, the declaration and the specification do not provide working examples, prediction, and guidance indicating that any changes in the non-conserved regions would have no deleterious effects on enzyme activity. The alignments in the Declaration of Dr. Satoshi Mori filed 11/23/2005 only show a relationship between the amino acid sequences of nicotianamine synthases from different biological sources.

The examiner respectfully disagrees with applicants' position that one of skill in the art need not be taught which amino acid residues can be changed without inactivating enzyme activity in view of the lack of working examples, prediction, and guidance showing which non-conserved amino acid residues can be changed without having any deleterious effects on enzyme activity. SEQ ID NO: 1 is disclosed by the specification as an amino acid sequence of 328 amino acid residues. The claims require at least 50% of SEQ ID NO: 1 to be altered, where at least 164 amino acid residues are changed (deletion, insertion, substitution, or combinations thereof) in SEQ ID NO: 1 and 101 amino acids must be conserved. One of ordinary skill in the art would have to make and search for proteins having these changes in the amino acid sequence and then determine by enzymatic assays whether the protein has nicotianamine synthase activity. Limiting the claims to recite the specific amino acid sequences of SEQ ID NOs: 23-28 does not overcome the rejection since no more than 32 amino acid residues are accounted for.

The amount of experimentation to make the nicotianamine synthase having 50% amino acid identity to SEQ ID NO: 1 comprising at least one of the recited amino acid sequences SEQ ID NOs: 23-28 is undue because of the lack of working examples, prediction, and guidance showing which non-conserved amino acid residues can be changed without inactivating enzyme activity. Such experimentation entails selecting any 164 amino acid residues in SEQ ID NO: 1 to change by amino acid deletion, insertion, substitution, and combinations thereof, and searching and screening for specific changes that will result in a functional nicotianamine synthase using enzyme assays. The specification's general teaching for using enzyme assays and characterization procedures shown in the Examples for searching and screening for the full scope of the nicotianamine synthases claimed is not guidance for making the claimed invention.

In view of the above considerations, the examiner maintains the position that specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make the invention commensurate in scope with these claims

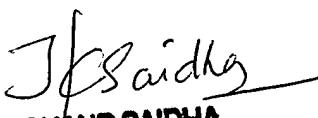
***Conclusion***

4. Claims 1, 35-38, and 41 are allowed.
5. Claims 29, 30, 39, 45, 46, 50, 51, 55, and 56 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
6. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).  
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.
8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR

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system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

  
TEKCHAND SAIDHA  
PRIMARY EXAMINER